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Abstract/Annual Report  
Year-1, AFOSR-F49620-92J1040  
George J. Mpitsos

During the past year, we have made progress in several areas of the proposed research:

(1) Computer simulations of catalytic networks. Andrade et al. (1993) have recently published the results of our first simulations, and have addressed the problem of the effect that catalytic error has in controlling system dynamics. Simulations of large networks are being designed in order to examine spatio-temporal dynamics in reaction-diffusion systems. The aim is to develop visualization and analysis methods to apply to large networks composed of biologically realistic neurons.

(2) Immunohistochemical studies have examined mammalian tissues that may be useful as model systems to examine distributed function in neurotransmission and neuromodulation (Soinila and Mpitsos, 1992; Soinila et al., 1992). It is necessary, as these and other publications (e.g., Mpitsos and Soinila, 1993) indicate, not only to understand neural organization in a "simple" animal, but also to examine the applicability of the findings to higher animals, and, if possible, to humans.

(3) Molecular biological studies of muscarinic receptors: In previous AFOSR-published work, Murray et al. (1985) and Murray and Mpitsos (1988) demonstrated the presence of muscarinic receptors in neural tissues of the sea slug *Pleurobranchaea*. Mpitsos et al. (1988) showed further that brief pharmacologic blocking of these receptors enhances 1-Trial associative learning. Over the past year, we have developed cloning vectors for generating fusion proteins to all of the five known muscarinic receptor subtypes in humans. Our next step is to obtain immunofluorescent antisera to the fusion proteins in order to visually identify cells containing the different muscarinic receptors. The in-between step will be to determine the specificity of the antisera. The findings will be applicable not only to our experimental animal, but also to studies of learning and pathologies in humans. The aim of this work, in conjunction with the neurophysiological and computer studies, is to understand (a) how particular neurotransmitters and neuromodulators affect the activity of neural assemblies, and (b) how individual transmitters act within the framework of the many neurochemical factors that impinge on the identified neural assemblies.

(4) Other studies. Inasmuch as the originally proposed budget was reduced by over one-third, we have not had sufficient woman/man-power to address two areas sufficiently. In one, the proposed computer-controlled training of animals in aquatic systems is still at the stage of software development, which I hope to have completed by the end of this year. In the second, the work on decomposition of extracellular records of spike trains to identify the activity interneurons that comprise the central pattern generator, and of all of the motor neurons that are activated by these interneurons, is so time-consuming that we have not had the resources to progress here as much as I would like. To facilitate the use of AFOSR funds, I generally apply the rule that the efforts in the laboratory must be directed toward experiments that make the greatest progress toward the fundamental goal of all of our work, namely to understand principles governing variable function in neural assemblies. As a result, work in areas that drain the efforts of the laboratory toward a single goal have to give way to other projects that appear to be generating more information.

New Publications:

Andrade, MA, Nuño, JC, Moran, F, Montero, F, Mpitsos, GJ (1993) Complex dynamics of a catalytic network having faulty replication into an error species. *Physica D*. In Press.

Mpitsos, GJ, Soinila, S (1993) In search of a unifying theory of biological organization: What does the motor system of a sea slug tell us about human motor integration? In *Variability and Motor Control*, (K. M. Newell, and D. Corcos, ed), Champaign: Human Kinetics. In press (April, 1993).

(A preprint of this, less edited, appeared in the 1991 Lecture Notes on Complex Systems, Santa Fe Institute; published in 1992)

Soinila, S, Bäck, N, Mpitsos, GJ (1992) Distribution of Met(5)-Enkephalin-Arg(6)-Gly(7)-Leu(8) immunoreactivity in the rat and mouse pituitary gland. *Regul. Pept.* 36: 271-282.

Soinila, S, Mpitsos, GJ, Soinila, J (1992) Enkephalin immunohistochemistry: Model studies on conjugation reaction and fixation. *J. Histochem. Cytochem.* 40: 231-239.

Additional Cited References.

Mpitsos, GJ, Murray, TF, Creech, HC, Barker, DL (1988) Muscarinic antagonist enhances One-trial food-aversion learning in *Pleurobranchaea*. *Brain Res. Bull.* 21: 169-179.

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Murray, TF, Mpitsos, GJ, Siebenaller, JF, Barker, DL (1985) Stereoselective L-[<sup>3</sup>H] Quinuclidinyl Benzilate-binding sites in nervous tissue of *Aplysia californica*: Evidence for Muscarinic Receptors. *J. Neurosci.* 5: 3184-3188.

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